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STIC-ILL

From: Citation@cas.org

Sent: Friday, November 26, 2004 4:59 PM

To: STIC-ILL

Subject: Pathogenesis (Haemophilia): "Production of Human IGG Monoclonal Antibodies Neutralizing the Functional Activity of Factor VIII by Immortalization of B Lymphocytes from a Haemophilia A Patient with Inhibitor."

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Title: Pathogenesis (Haemophilia): "Production of Human IGG Monoclonal Antibodies Neutralizing the Functional Activity of Factor VIII by Immortalization of B Lymphocytes from a Haemophilia A Patient with Inhibitor."

Author(s):

Source: Blood Weekly, (9 Sep 1996) pp. N/A. ISSN: 1065-6073.

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## STIC-ILL

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**From:** Citation@cas.org  
**Sent:** Friday, November 26, 2004 5:00 PM  
**To:** STIC-ILL  
**Subject:** Pathogenesis (Haemophilia): "Production of Human IGG Monoclonal Antibodies Neutralizing the Functional Activity of Factor VIII by Immortalization of B Lymphocytes from a Haemophilia A Patient with Inhibitor."

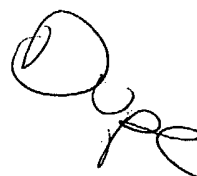
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571 272-0845  
[maher.haddad@uspto.gov](mailto:maher.haddad@uspto.gov)



**Comments**

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**"Production of Human IGG Monoclonal Antibodies Neutralizing the Functional Activity of Factor VIII by Immobilization of B Lymphocytes from a Haemophilia A Patient with Inhibitor."**

Blood Weekly, September 9, 1996, p.17

DOCUMENT TYPE: Research News LANGUAGE: English

RECORD TYPE: FULLTEXT

AUDIENCE: Professional

Word Count:

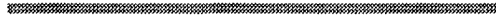
373

TEXT: According to an abstract submitted by the authors to the 22nd International Congress of the World Federation of Hemophilia, held June 23-28, 1996, in Dublin, Ireland, "Eight to 20% of haemophilia A patients produce antibodies neutralizing the activity of infused factor VIII. Determination of the specificity of those antibodies is a critical requisite for the understanding of the mechanisms sustaining immune response towards FVIII and the design of new therapies to inhibit the activity of anti-FVIII antibodies or suppress their production. So far, the analysis of the specificity of anti-FVIII antibodies has been carried out with human polyclonal antibodies which is rendered difficult by the large repertoire of those antibodies. Such study would be greatly facilitated by the use of human monoclonal anti-FVIII antibodies provided the monoclonal antibodies reflect exactly the repertoire of the patient's antibodies. For this purpose we have established cell lines producing human IgG anti-FVIII monoclonal antibodies by immortalizing with the Epstein Barr virus B lymphocytes from a hemophilia A patient with inhibitor. Lymphocytes were purified from the blood of the hemophilia A patient with known inhibitor and immortalized by infection with Epstein-Barr virus. Supernatants were screened in ELISA for the presence of IgG anti-FVIII antibodies. Cell lines in positive wells were expanded and cloned. The selection of cell lines producing antibodies of the IgG isotype ensures that the antibodies accurately reflect the specificity of the patient's immune response. Indeed IgG antibodies are produced by memory B lymphocytes by opposition to IgM antibodies that are produced mostly by naive B cells. The supernatants of immortalized cell lines producing IgG anti-FVIII antibodies were then tested for their ability to inhibit FVIII activity. Two cell lines producing neutralizing anti-FVIII antibodies were expanded and subcloned. Both cell lines recognized the light chain of FVIII on Western blot as did the polyclonal antibodies present in the patients plasma. These results indicate that the production of human monoclonal antibodies by the Epstein-Barr virus technique is a promising approach to study FVIII inhibitor." (Authors) B. Desqueper, M. Jacquemin, J. Arnout, M. DiGiambatista, J.G. Gilles, R. Laub, K. Peerlinck, J. Vermeylen and J.-M. Saint-Remy. (Institution) Center for Molecular and Vascular Biology, Leuven, Belgium.

DESCRIPTORS: news

SUBJECT HEADING: Pathogenesis (Haemophilia)

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FILE 'DISSABS, 1MOBILITY, AGRICOLA, AQUASCI, BIOTECHNO, COMPENDEX,  
COMPUAB, CONF, CONFSCI, ELCOM, HEALSAFE, IMSDRUGCONF, LIFESCI, MEDICONF,  
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ADISNEWS, ANABSTR, ANTE, AQUALINE, BIOBUSINESS, ...' ENTERED AT 16:10:30  
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L1	32 S LE2E9
L2	11 DUP REM L1 (21 DUPLICATES REMOVED)
L3	22 S KRIX (A) 1
L4	14 DUP REM L3 (8 DUPLICATES REMOVED)
L5	69 S BO2C11
L6	26 DUP REM L5 (43 DUPLICATES REMOVED)
L7	47166 S HUMAN (A) ((MONOCLONAL ANTIBOD?) OR MAB)
L8	47 S (L7 (S) FVIII)
L9	19 DUP REM L8 (28 DUPLICATES REMOVED)

ACCESSION NUMBER: 96:474329 PROMT  
TITLE: Pathogenesis (Haemophilia): "Production of Human IGG Monoclonal Antibodies Neutralizing the Functional Activity of Factor VIII by Immortalization of B Lymphocytes from a Haemophilia A Patient with Inhibitor."  
SOURCE: Blood Weekly, (9 Sep 1996) pp. N/A.  
ISSN: 1065-6073.  
LANGUAGE: English  
WORD COUNT: 359

\*FULL TEXT IS AVAILABLE IN THE ALL FORMAT\*

AB B. Desqueper, M. Jacquemin, J. Arnout, M. DiGiambatista, J.G. Gilles, R. Laub, K. Peerlinck, J. Vermylen and J.-M. Saint-Remy. Center for Molecular and Vascular Biology, Leuven, Belgium.

According to an abstract submitted by the authors to the 22nd International Congress of the World Federation of Hemophilia, held June 23-28, 1996, in Dublin, Ireland, "Eight to 20% of haemophilia A patients produce antibodies neutralizing the activity of infused factor VIII. Determination of the specificity of those antibodies is a critical requisite for the understanding of the mechanisms sustaining immune response towards **FVIII** and the design of new therapies to inhibit the activity of anti-**FVIII** antibodies or suppress their production. So far, the analysis of the specificity of anti-**FVIII** antibodies has been carried out with human polyclonal antibodies which is rendered difficult by the large repertoire of those antibodies. Such study would be greatly facilitated by the use of human monoclonal anti-**FVIII** antibodies provided the monoclonal antibodies reflect exactly the repertoire of the patient's antibodies. For this purpose we have established cell lines producing human IgG anti-**FVIII** monoclonal antibodies by immortalizing with the Epstein Barr virus B lymphocytes from a hemophilia A patient with inhibitor. Lymphocytes were purified from the blood of the hemophilia A patient with known inhibitor and immortalized by infection with Epstein-Barr virus. Supernatants were screened in ELISA for the presence of IgG anti-**FVIII** antibodies. Cell lines in positive wells were expanded and cloned. The selection of cell lines producing antibodies of the IgG isotype ensures that the antibodies accurately reflect the specificity of the patient's immune response. Indeed IgG antibodies are produced by memory B lymphocytes by opposition to IgM antibodies that are produced mostly by naive B cells. The supernatants of immortalized cell lines producing IgG anti-**FVIII** antibodies were then tested for their ability to inhibit **FVIII** activity. Two cell lines producing neutralizing anti-**FVIII** antibodies were expanded and subcloned. Both cell lines recognized the light chain of **FVIII** on Western blot as did the polyclonal antibodies present in the patients plasma. These results indicate that the production of **human monoclonal antibodies** by the Epstein-Barr virus technique is a promising approach to study **FVIII** inhibitor."

THIS IS THE FULL TEXT: COPYRIGHT 1996 Charles W HendersonAccording . . . of the specificity of those antibodies is a critical requisite for the understanding of the mechanisms sustaining immune response towards **FVIII** and the design of new therapies to inhibit the activity of anti-**FVIII** antibodies or suppress their production. So far, the analysis of the specificity of anti-**FVIII** antibodies has been carried out with human polyclonal antibodies which is rendered difficult by the large repertoire of those antibodies. Such study would be greatly facilitated by the use of human monoclonal anti-**FVIII** antibodies provided the monoclonal antibodies reflect exactly the repertoire of the patient's antibodies. For this purpose we have established cell lines producing human IgG anti-**FVIII** monoclonal antibodies by immortalizing with the Epstein Barr virus B lymphocytes from a hemophilia A patient with inhibitor. Lymphocytes were. . . with known inhibitor and immortalized by infection with Epstein-Barr virus. Supernatants were screened in ELISA for the presence of IgG anti-**FVIII** antibodies.

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